SUPPORT FOR THE AMENDMENT

Claims 1-6, 8-10 and 12 are pending. Claims 1-6, 10 and 12 are currently amended. Claims 7 and 11 are canceled without prejudice. Claims 1, 3, 5, 6 and 10 are amended to include a pressure limitation of "1 to 1000 Pa" as supported in the specification: page 13, lines 4-8. Claim 10 is amended to incorporate the subject matter of original claim 11 and finds further support in the specification: page 14, lines 9-22, and the Examples. All amended claims have been amended for grammatical purposes as well. No new matter has been entered.

REMARKS/ARGUMENTS

Claims 1, 2, 5 and 7-11 are rejected under §102(b) as anticipated by *Talton*. Claims 3, 4, 6 and 12 are rejected under §103(a) as obvious in view of *Talton*. Applicants respectfully traverse these rejections.

Non-Product-By-Process Claims (5, 6, 8-10 and 12)

The current independent claims 5, 6 and 10 require that the irradiating of a solid target with a laser beam be performed "under an ambient pressure of 1 to 1000 Pa". *Talton* discloses a pulsed laser deposition operation that is performed under a pressure of about 10 Torr (equal to 1330 Pa) or higher (Abstract), and the use of a coating chamber at a pressure of around atmospheric pressure (e.g., 760 Torr), which may be a pressure of about 10 Torr to as high as about 2500 Torr (page 14, lines 20-22). These pressure ranges of *Talton* (i.e., 1330 Pa or higher), are clearly not within or touching the range as claimed by Applicants (i.e., 1-1000 Pa). Additionally, the apparatus of claim 10 includes a "vibrating device for intermittently applying vibration to the excipient particles". However, *Talton* is silent with respect to a vibrating device. Accordingly, *Talton* does not anticipate Applicants' claims (i.e., 5, 6, 8-10 and 12).

Furthermore, Applicants submit that *Talton* does not render obvious said claims. With respect to the methods of manufacturing a medical agent of claims 5 and 6, the medical agent exhibits the following unexpected results as described by the current specification: "[S]ince the prepared drug nanoparticle or the drug-protein composite nanoparticle are directly coated onto the excipient thereby to produce a composite medical agent, a scattering or a re-agglomeration of the nanoparticles can be effectively suppressed. As a result, a problem regarding handling property of the nanoparticles can be effectively solved." (page 10, lines 18-23). Moreover, *Talton* and present claims 5 and 6 differ in that the particles of

Talton are core particles which can be a medical agent, whereas the nanoparticles as claimed by Applicants are drugs and are adhered to the surface of the core particles. *Talton* does not disclose or suggest coating materials as drug nanoparticles having an average diameter of 100 nm or less as claimed by Applicants (see a list of "coating compositions", page 43, *Talton*). Thus, *Talton* does not render obvious present claims 5 and 6.

With respect to the apparatus of claim 10 comprising a vibrating device, the apparatus exhibits the following unexpected results as described by the current specification: "When the vibrations are continuously or intermittently applied to the excipient particles (base material particles) or the like by the vibrating device, the base material particles are fluidized and a surface direction of each of the excipient particles is changed during the vibration, so that the thin film layer composed of the drug nanoparticles can be uniformly adhered and formed onto the entire surfaces of the respective excipient particles." (page 14, lines 17-22). Moreover, *Talton* and preset claim 10 differ in that *Talton* uses a fluidizing method in which the core particles are fluidized by flowing air and the core particles are continuously fluidized, whereas Applicants use a vibrating device for intermittently applying vibration for fluidizing nanoparticles and depositing them on core particles. When the core particles are continuously applied with vibrations, it is difficult to coat the nanoparticles onto the surface of the core particles, causing a decrease in production efficiency, and the nanoparticles of *Talton* are unavoidably carried by the strong air flow and discharged from the coating chamber without adhering to the surface of the core particles. *Talton* does not disclose or suggest Applicants' apparatus comprising a vibrating device for intermittently applying vibration so that the nanoparticles are fluidized and deposited on the core particles. Thus, *Talton* does not render obvious present claim 10.

Product-By-Process Claims (1-4)

The current independent claims 1 and 3 require that the irradiating of a solid target with a laser beam be performed "under an ambient pressure of 1 to 1000 Pa". As discussed above, *Talton* does not disclose pressure ranges within or touching the range as claimed by Applicants.

With respect to the product-by-process claims of the presently claimed invention, the courts have enunciated that: "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claims is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985).

There are two important aspects to the foregoing. First, the products must be identical or an obvious variant thereof. Second, patentability of a product may not depend on its method of production, but the method of production cannot be disregarded if that method provides a distinct structural characteristic or product.

First, Applicants point out that with respect to present claim 1, the resulting drug nanoparticles having a nano-size have the following beneficial characteristics: improved drug delivery, improved effect of the drug, and suppression of adverse effects of the drug (specification: page 6, lines 6-9). With respect to present claim 3, the resulting drug-protein nanocomposites comprising drug and protein nanoparticles have the following beneficial characteristics: improved permeability of the drug at the cell membrane and improved bioavailability of the drug (specification: page 6, line 19, to page 7, line 1).

Further and with respect to present claim 1, Applicants submit that the structure of the present invention and that of *Talton* is different for the following reasons. Immediately after

a laser beam is irradiated to a solid target, the components of the target are released as refined components in the form of molecules and clusters. However, for example, in a case where the refined components are coated onto core particles, the refined components collide with molecules of gases contained in the ambient during a time until the released components reach the core particles, so that the refined components are aggregated to each other to grow to be a large-sized particle. In this case, the higher the ambient gas pressure is set, the larger the aggregated particle is disadvantageously grown. Therefore, in order to make particles on a nano-size level like that of the present invention (i.e., having an average diameter of 100 nm or less), the deposition operation is performed under a pressure of 1 to 1000 Pa. Additionally and for argument sake only, assuming that one skilled in the art would conduct the manufacturing method of the present invention under the pressure condition of *Talton* (i.e., 10 Torr or higher), the resultant drug particles would have an incomparably large diameter. Accordingly, the drug nanoparticle of claim 1 has a distinct structural characteristic (i.e. size) in comparison with *Talton*, thus rendering it both non-anticipated and non-obvious for all the reasons discussed above.

Further and with respect to claim 3, Applicants submit that the structure of the present invention and that of *Talton* is different for the following reasons. *Talton* discloses that "Coating the core materials with the bladed particulate target material may result in coated particles having average diameters of less than about 1 mm, less than about 100 microns, or less than about 10 microns" (page 7, lines 1-3). *Talton's* disclosure envisions coated particles having diameters in the millimeter and micron ranges that are greatly larger than those of the present invention ($1x10^{-6}$ m versus $1x10^{-9}$ m). In addition and as discussed above, in order to make particles on a nano-size level like that of the present invention (i.e., having an average diameter of 100 nm or less), the deposition operation is performed under a pressure of 1 to 1000 Pa, which is significantly lower than that of *Talton*. Therefore, *Talton's* huge particles

do not disclose or suggest the Applicants' nanoparticles, and they also do not and cannot exhibit the same improved permeability and bioavailability of the drug-protein nanocomposite of the present invention (see above). Accordingly, *Talton* does not render obvious Applicants' nanocomposite of claim 3 having drug and protein nanoparticles with an average diameter of 100 nm or less.

Conclusion

For the reasons discussed above, Applicants submit that all now-pending claims are in condition for allowance. Applicants respectfully request the withdrawal of the rejections and passage of this case to issue.

Respectfully submitted,

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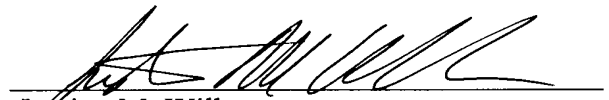

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